Complications of cesarean deliveries among HIV-infected women in the United States

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Abstract

Objective—To compare rates of complications associated with cesarean delivery in HIV-infected and HIV-uninfected women in the United States and to investigate trends in such complications across four study cycles spanning the implementation of HAART in the United States (1995–1996, 2000–2001, 2005–2006, 2010–2011).

Design—The Nationwide Inpatient Sample from the Healthcare Cost and Utilization Project is the largest all-payer hospital inpatient care database in the United States; when weighted to account for the complex sampling design, nationally representative estimates are derived. After restricting the study sample to women aged 15–49 years, our study sample consisted of approximately 1 090 000 cesarean delivery hospitalizations annually.

Methods—Complications associated with cesarean deliveries were categorized as infection, hemorrhage, or surgical trauma, based on groups of specific International Classification of Diseases 9th revision codes. Length of hospitalization, hospital charges, and in-hospital deaths were also examined.

Results—The rate of complications significantly decreased during the study periods for HIV-infected and HIV-uninfected women. However, rates of infectious complications and surgical trauma associated with cesarean deliveries remained higher among HIV-infected, compared with HIV-uninfected women in 2010–2011, as did prolonged hospital stay and in-hospital deaths. Length of hospitalization decreased over time for cesarean deliveries of HIV-infected women to a greater extent compared with HIV-uninfected women.

Conclusion—In the United States, rates of cesarean delivery complications decreased from 1995 to 2011. However, rates of infection, surgical trauma, hospital deaths, and prolonged hospitalization are still higher among HIV-infected women. Clinicians should remain alert to this persistently increased risk of cesarean delivery complications among HIV-infected women.

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Keywords

AIDS; cesarean section; HAART; HIV; obstetric labor complications

Introduction

Similar to overall trends in cesarean delivery rates in the United States, the proportion of HIV-infected women having a cesarean delivery has increased in recent years [1–3]. This is likely due, in part, to the role of cesarean delivery in reducing the risk of mother-to-child transmission (MTCT) of HIV type 1. Research conducted in the 1990s demonstrated that cesarean delivery performed prior to the onset of labor and prior to the rupture of the amniotic membranes can substantially reduce the risk of MTCT of HIV [4,5]. As such, the American College of Obstetricians and Gynecologists and the US Public Health Service recommend that HIV-infected women with plasma viral loads higher than 1000 copies/ml be counseled on the benefits of cesarean delivery performed at 38 weeks gestation to prevent MTCT of HIV [6,7]. Scheduled cesarean deliveries performed for HIV prevention are a subset of elective cesarean deliveries, which are generally performed at 39 weeks (before onset of labor) and may include those performed for medical or obstetrical indications as well as those performed upon maternal request [8].

Several studies have demonstrated that HIV-infected women are at increased risk of perioperative morbidity from cesarean delivery compared with HIV-uninfected controls [9–16], and their risk for morbidity is higher with cesarean as compared with vaginal delivery [4,9,17–19]. Most of this increased risk for morbidity is related to infection (e.g., urinary tract infection, pneumonia, wound infection, septicemia), which is elevated for all women undergoing cesarean delivery [20], such that the risks are greatest for cesarean deliveries performed after onset of labor or ruptured membranes, intermediate with scheduled cesarean delivery, and lowest with vaginal delivery [21]. Although the studies upon which existing US guidelines were made demonstrate a clear benefit in reducing MTCT that outweighs potential risks of morbidity, most were conducted before the widespread use of HAART [21–23]. As maternal viral load is significantly associated with risk of MTCT [24–30], the additional benefit of scheduled cesarean delivery when full viral suppression has been achieved through the use of HAART has been questioned [31–33], and the US guidelines, as mentioned, do not recommend elective cesarean delivery in women with undetectable viral load [4,5].

Given that perioperative morbidity associated with cesarean delivery is correlated with the degree of immunosuppression [9–13,17,30], the risks for morbidity may be lower for HIV-infected women on HAART. Furthermore, as any elevation in morbidity associated with cesarean deliveries needs to be balanced against benefits of preventing MTCT in the era of HAART, research is needed to assess the extent to which cesarean delivery continues to be associated with increased risk of complications. This study addresses the question of whether morbidity rates associated with cesarean delivery have declined for HIV-infected women with the widespread use of HAART in the United States. More specifically, we conducted a large US population-based analysis of hospitalization data, using the

Nationwide Inpatient Sample (NIS) database to test two hypotheses: (i) that the rate of complications associated with cesarean deliveries among HIV-infected women has declined from 1995–1996 (pre-HAART) to 2000–2001 (early combination- HAART), 2005–2006, and 2010–2011 (both times of widespread use of combination HAART); and (ii) that complications associated with cesarean delivery in HIV-infected women have declined to a greater degree, compared with HIV-uninfected women, from 1995–1996 to 2010–2011.We also evaluated changes in rates of cesarean deliveries and elective cesarean deliveries among HIV-infected, compared with HIV-uninfected women in the United States over time.

Methods

Data source and definition of exposures and outcomes

The NIS of the Agency for Healthcare Research and Quality is the largest all-payer hospital inpatient care database in the United States providing a wide range of information on hospitalizations. It is a stratified probability sample of approximately 20% of all US community hospitals on the basis of five characteristics: geographic region, ownership, rural/urban location, teaching status, and bed size. Before 2005, the American Hospital Association (AHA) defined community hospitals as nonfederal, short-term (average stay <30 days) general, and specialty hospitals open to the public. In 2005, the AHA added long-term acute care facilities (stays >25 days) to the definition of community hospitals [34].

The NIS includes all discharges from selected hospitals and provides information on 5 to 8 million hospital stays from an average of 1000 hospitals each year. Each record is weighted to account for the complex sampling design and when weighted, nationwide estimates can be derived [34]. To track changes in cesarean delivery-associated complications in conjunction with increasing use of HAART, this analysis includes data from 1995 to 1996, 2000 to 2001, 2005 to 2006, and 2010 to 2011. For these years, we identified all pregnancy hospitalizations that resulted in a delivery by using *International Classification of Diseases, 9th revision, Clinical Modification* (ICD-9-CM) codes 650, and V27, procedure codes of 720–721, 722.1, 722.9, 723.1, 723.9, 724, 725.1–725.4, 726, 727.1, 727.9, 728–729, 732.2735.9, 736, 740–742, 744, and 749.9, and diagnosis-related group codes of 370–375. The ICD-9 algorithm developed by Gregory *et al.* [35] was used to identify cesarean deliveries and determine if they were elective. An elective cesarean delivery was defined as a procedure that occurred prior to the onset of labor (defined by ICD-9-CM codes 652.1, 653, 656.3, 659.0, 659.1, 660–662, 663.0) without regard to previous history of cesarean delivery; repeat cesarean deliveries were categorized as elective per the modified algorithm by Meikle *et al.* [8].

Our primary outcomes included occurrence of at least one cesarean delivery-associated complication, occurrence of specific cesarean delivery-associated complications, extended hospital stay (>7 days), hospital charges, and deaths during hospitalization. All in-hospital deaths were included regardless of length of stay. We defined the specific cesarean delivery-associated complications as follows:

1. Infection, including pneumonia (ICD-9-CM codes 486, 507.0–507.8, 514); urinary tract infection, including acute pyelonephritis (599.0, 590.9, 646.64 760.1, 590.1);

and other infections, including genital tract and pelvic infection (639.0), postoperative infection and other complications of obstetrical surgical wounds (998.59, 998.5, 674.34, 674.14), wound dehiscence (998.31), sepsis, septicemia, and other infection (670.24, 995.91, 995.92, 038, 999.3), major puerperal infection (670.04, 670.84), puerperal endometritis (670.14), unspecified inflammatory disease of the uterus (615.9), thrombophlebitis (670.34), and fever (780.60, 672.04).

2. Hemorrhage, including postpartum hemorrhage (666.14, 666.24, 661.24, 666.34), blood transfusion (V58.2), and acute posthemorrhagic anemia (285.1).

3. Thrombosis, including deep thrombophlebitis (671.44), obstetrical pulmonary embolism and deep vein thrombosis (673.04, 673.24), obstetrical pyemic and septic embolism (67673.34), other pulmonary embolism (673.84).

4. Surgical trauma, including obstetrical injury to pelvic organs (665.54), small bowel obstruction or ileus (560.9, 560.1), obstetrical pelvic hematoma (665.74), unspecified obstetrical trauma (665.94), and non-healing surgical wound (998.83).

'Any complication' included any of the four complications above.

Statistical analysis

Our primary independent variables were HIV status and year of hospitalization; subanalyses were conducted to assess differences by HIV status among all cesarean deliveries and elective cesarean deliveries as defined above. To identify women infected with HIV, we used ICD-9-CM codes: 042, 079.53, 279.10, 279.19, 795.71, 795.8, and V08 [36]. Patient age, primary expected payer (indicator of socioeconomic status), hospital teaching status/ location, alcohol/substance abuse (ICD-9 codes 291–292, 303, 305, 648.3, 655.5, 965.0, V65.42), anemia (ICD-9 codes 648.2, 280–285), and diabetes (preexisting and gestational) (ICD-9 codes 250, 648.0, 648.8, 790.29, 791.5) were included as possible confounders, because they have been previously associated with complications related to cesarean delivery among HIV-infected women [19,30]. Race was not examined because it is often not reported by states or there are inconsistencies and missing values. For 1995 and 2010 (pre-HAART and recent HAART eras, respectively) we compared the distribution of these characteristics among HIV-infected and HIV-uninfected women for all cesarean deliveries and for elective cesarean deliveries. Differences were evaluated with chi-square tests (alpha = 0.05).

For 1995–1996 and 2010–2011, we compared the rate of each complication per 1000 deliveries among HIV-infected and HIV-uninfected women for cesarean deliveries overall, and separately for elective cesarean deliveries. Differences in complication rates for HIV-infected and HIV-uninfected women were assessed with the Student's t-test (alpha = 0.05). As there were very few thrombotic events, resulting in unstable estimates, these results are not presented. Multivariable logistic regression models were used to assess the odds of each complication for HIV-infected vs. HIV-uninfected women, adjusting for patient age, primary expected payer, hospital teaching status/location, anemia, diabetes, and alcohol/ substance abuse [19,30].

To further assess trends in complications over time, we compared data across four study periods: 1995–1996 (reference period), 2000–2001, 2005–2006, and 2010–2011, in multivariable logistic regression models, stratified by HIV status. We used 2-year periods to derive stable estimates, given the small number of outcomes in some categories per year, adjusting for the same potential confounders. Additionally, we evaluated differences in trends among HIV-infected and HIV-uninfected women over time by including an interaction term of study period and HIV status in a multivariable logistic regression model, and testing the significance of the interaction term. To assess trends in mean hospital charges for cesarean deliveries by HIV status, multiple linear regression was performed adjusting for the same potential confounders Hospital charges were adjusted for inflation using the Bureau of Labor Statistics' Consumer Price Index.

A sensitivity analysis was performed to examine the effect of changes in the distribution of primary vs. repeat elective cesarean delivery over the study period. A repeat cesarean delivery was defined using ICD-9-CM code 654.2

Results

There were a total of 2798 estimated cesarean deliveries among HIV-infected women and 1 270 952 among HIV-uninfected women in the United States in 2010; this represents 58.5% of all deliveries among HIV-infected women for that year, compared with 33% for HIV-uninfected women ($P < 0.0001$). The number of cesarean deliveries among HIV-infected women in the United States steadily increased from 934 in 1995 to 2290 in 2000 to 2354 in 2005; representing 19.6, 49.9, and 57.5% of all deliveries among HIV-infected women, respectively. In contrast, among HIV-uninfected women, the respective proportions of deliveries that were cesarean deliveries were 21, 22.8, and 31.1%. Since 2000, the great majority of cesarean deliveries among HIV-infected women were elective (44.6% in 1995, 88.9% in 2000, 91.5% in 2005, and 90.9% in 2010). The corresponding proportions for elective cesarean delivery among HIV-uninfected women were 46.1% in 1995, 62% in 2000, 70.3% in 2005, and 73.1% in 2010.

HIV-infected women had a higher prevalence of anemia and alcohol/substance abuse compared with HIV-uninfected women for all years studied. HIV-infected women were more likely to have public payer insurance, delivery at an urban teaching hospital and be located in the South compared with HIV-uninfected women undergoing a cesarean delivery, for all years studied (1995 and 2010 data shown in Table 1). Cesarean delivery hospitalizations of HIV-infected women were, on average, slightly longer for all years studied and were associated with higher mean hospital charges in 1995 ($P < 0.001$), 2000 ($P = 0.003$), and 2010 ($P < 0.001$) (Table 1).

The rate of any complications associated with cesarean delivery in 2010–2011 was 116.6/1000 deliveries among HIV-infected women in the Unites States, compared with 67.9/1000 deliveries among HIV-uninfected women. In 1995–1996, the corresponding rates for HIV-infected and HIV-uninfected women were 210.6/1000 deliveries and 118.9/1000 deliveries, respectively (Table 2). Compared with HIV-uninfected women, cesarean deliveries of HIV-infected women in 2010–2011 had greater odds of being associated with

infectious complications (adjusted odds ratios [aOR], 1.66; 95% confidence interval [CI]: 1.18–2.35), surgical trauma (aOR, 2.45; 95% CI, 1.41–4.26) and extended hospitalizations (aOR, 2.09, 95% CI: 1.58–2.74). Even though a rare outcome, cesarean deliveries of HIV-infected women had greater odds of resulting in death, compared with those of HIV-uninfected women (aOR, 9.06, 95% CI, 2.60–31.58) (Table 2). With the exception of surgical trauma, similar relationships were observed in 1995–1996 (Table 2). As almost all cesarean deliveries among HIV-infected women in 2010–2011 were elective, the relationships mentioned above were also seen in the respective comparisons of elective cesarean delivery complication rates (Table 2).

For all women, the rate of infections among cesarean deliveries decreased from 1995 to 2010 with a similar pattern among the HIV-infected and HIV-uninfected women (Fig. 1). The rate of surgical trauma among cesarean deliveries of HIV-uninfected women decreased over the study period, whereas the rate of surgical trauma among cesarean deliveries of HIV-infected women increased. Among HIV-uninfected women, the odds of any complication, each of the complication types, extended hospital stay and deaths associated with cesarean delivery significantly decreased over the study period, with most of the decrease occurring by 2005–2006, (Table 3). In contrast, among HIV-infected women, significant decreases were only observed for infection or any complication beginning in 2005–2006, and for prolonged hospital stay during each of the periods of observation; again, little or no additional decrease occurred in the final year of observation (Table 3). The decreases for elective cesarean delivery complications mirrored those observed for all cesarean deliveries (Table 3). There was no statistically significant interaction of HIV status and study period for any complication, infection, hemorrhage, and death. There was a marginally significant interaction of HIV status and time for surgical trauma ($P = .07$), and a significant interaction for extended hospital stay ($P = 0.02$). The odds of an extended hospital stay decreased since 1995 to a greater extent for cesarean deliveries of HIV-infected women (Table 3). For all cesarean deliveries, adjusted mean charges (in 2010 $) for HIV-infected women were $15 793 in 1995–1996 and were not significantly different in 2000–2001 or 2005–2006 but were higher in 2010–2011, when adjusted mean charges were $24 104 ($P < 0.001$). For HIV-uninfected women, mean charges increased significantly at each time period compared with the referent time period of 1995–1996 (Table 3). This pattern was identical in women with elective cesarean deliveries.

The sensitivity analysis of primary vs. repeat cesarean deliveries showed a slight increase in the proportion of repeat cesarean deliveries among all elective deliveries from 1995–2010 among the HIV-uninfected women (from 57 to 60%), but a slight corresponding decrease among HIV-infected women (from 56 to 53%); there were some fluctuations for in-between years among the HIV-infected women (results not shown). Overall, complication rates were slightly higher for primary, compared with repeat, elective cesarean deliveries, but these differences were mostly not statistically significant among the HIV-infected women. The trends in complications over time per type of elective cesarean delivery mirrored those observed for elective cesarean deliveries overall (results not shown).

Discussion

In this analysis of multiple years of nationally representative US hospitalization data, we find that the rates and adjusted odds of infectious complications, surgical trauma, prolonged hospitalization and in-hospital deaths remain higher among HIV-infected, compared with HIV-uninfected, women undergoing a cesarean delivery, even in the era of widespread use of HAART during pregnancy. With the exception of surgical trauma, rates of these complications have decreased in both HIV-infected and HIV-uninfected women over the 15-year study period encompassing the implementation of HAART, and appear to have plateaued over the past several years. However, the rate of extended hospital stay decreased to a greater extent for cesarean deliveries of HIV-infected women.

Most studies examining whether morbidity associated with elective cesarean delivery has declined in parallel with changes in the management of HIV during pregnancy were conducted during the integration of antiretroviral monotherapy into practice and ended just as combination therapies were being introduced [9,17,19]. Only a few more recent studies have focused on women receiving HAART. In two small studies comparing HIV-infected women to HIV-uninfected controls, the difference in major complications between the two groups (severe anemia, need for postpartum surgical procedures, pneumonia, peritonitis, sepsis, thrombosis, diffuse intravascular coagulation and subileus/ileus) was not significant [30,37], although one of the studies did find differences in minor complications (mild anemia, urinary tract infections, fever), the length of hospital stays, and blood loss [37]. Given that major complications are rare, these smaller studies were insufficiently powered to evaluate the comparative frequencies for the more severe outcomes. In a third population-based recent study of HIV-infected women in France, complication rates were lower following vaginal, compared with cesarean delivery; complications were mainly infections or hemorrhage [38]. Whereas the unadjusted rate of hemorrhage was higher among HIV-infected women in this study, when adjusting for sociodemographic factors and underlying morbidity the risk became lower, compared with HIV-uninfected women.

A recent meta-analysis pooling data from four studies conducted in Europe and the United States (1995–2007) demonstrated that among women who had a cesarean delivery HIV infection was associated with six times the risk of puerperal sepsis compared with HIV-uninfected women [39]. Among 10 studies containing information on wound infection conducted in Africa, Europe and the United Studies from 1995 to 2010, the pooled odds ratio [OR] for this outcome, comparing HIV-infected to HIV-uninfected women, was 1.75 (CI: 1.20–2.55) [39]. Twelve studies examining endometritis (conducted in Africa, Europe, the United States, and Thailand, 1995–2010) showed that HIV-infected women had over double the odds of endometritis than HIV-uninfected women. One study that examined the association between HIV and postpartum hemorrhage among women having a cesarean delivery found no association [40].

The current study has the largest number of observations from any single study, and the results reflect data that are nationally representative for the United States. Our findings confirm a persistently elevated risk of complications, mostly infection, associated with cesarean delivery among HIV-infected women, even in the combination antiretroviral era.

Although a study suggested that the higher complication risk was only for women with CD4$^+$ cell count below 500 cells/μl [30], a higher rate of complications was seen even in women without immune deficiency in a French study [8]; we could not examine this factor, as information on CD4$^+$ cell counts is not available in NIS.

We observed an increase in the proportion of cesarean deliveries among all deliveries of HIV-infected women in the United States over the period of observation; the proportion for 2010, 58%, was almost double the corresponding proportion for HIV-uninfected women. The great majority of these cesarean deliveries (over 90%) were elective, likely because of clinical guidelines recommending a prelabor cesarean delivery for HIV-infected women, unless their HIV viral load is less than 1000 copies/ml at 34 weeks gestation. Although it is possible that some women with viral load less than this cutoff may still undergo cesarean delivery, as most HIV-infected women in the United States are now on HAART regimens during pregnancy and achieve virologic suppression by their third trimester [41,42], the proportion of HIV-infected women undergoing cesarean delivery in the United States may decline. Indeed, in France the rate of elective cesarean delivery decreased since 2000 [31]; this has also been reported elsewhere in Europe [26]: The proportion of cesarean delivery in the French perinatal cohort was 52.9% in 2005 through 2010, which was twice the general French cesarean delivery rate [38]. In the same cohort, the proportion of elective cesarean trended from 56% in 2000 to 41% in 2004, whereas that for emergency cesarean section was stable at 29% [23]. In the European Collaborative study, the elective cesarean delivery rate for HIV-infected women declined from 67% in 1999–2001 to 51% by 2005–2007, whereas the emergency cesarean rate ranged from 15 to 17% in the HAART era [24].

Another obstetrical practice trend during this time period in the United tates which may account for some of the increases in elective cesarean deliveries observed (in both HIV-infected and HIV-uninfected women) is the decrease in the rate of vaginal births after cesarean [43]. Our sensitivity analysis, however, did not demonstrate marked differences in the distributions of primary vs. repeat elective cesareans over time, or differences in complication rates per elective cesarean type.

This study has some limitations. NIS contains administrative data and lacks information on CD4$^+$ cell count or receipt of ART; we based assumptions on the general utilization patterns of HAART among pregnant women in the United States over time. Some women may have not been tested for HIV or may have been unaware of their HIV status and thus misclassified as HIV-uninfected. Additionally, administrative data are affected by coding practices and may be subject to errors or omissions. We are unable to separate the elective cesarean deliveries that were performed for HIV prevention (i.e. scheduled cesarean deliveries) from those performed in HIV-infected women for another indication. This analysis may be limited in that estimates for surgical trauma and in-hospital death were based on few events in the HIV-infected women which may lead to unstable estimates. Finally, general changes in medical practices and in coding patterns may affect the study of trends over time; the study of HIV-uninfected women as the comparison group provides a measure of general trends in such practices, even though the contribution of particular factors is impossible to discern.

In conclusion, despite declining over time, rates of infectious complications, surgical trauma and in-hospital deaths associated with cesarean delivery remain higher for HIV-infected, compared with HIV-uninfected women in the United States. Additionally, the overall proportion of cesarean deliveries among HIV-infected women's deliveries has not decreased in the United States. The persistently elevated risk of cesarean delivery complications needs to be further evaluated among large cohorts of women at different stages of HIV disease and degrees of virologic suppression. Such risks need to be carefully weighed against any additional benefit in reduction in MTCT of HIV infection for women who are already on HAART regimens with good virologic suppression, in order to optimize the health of the mother–infant dyad.

Acknowledgements

References

1. Dominguez KL, Lindegren ML, D'Almada PJ, Peters VB, Frederick T, Rakusan TA, et al. Increasing trend of Cesarean deliveries in HIV-infected women in the United States from 1994 to 2000. J Acquir Immune Defic Syndr. 2003; 33:232–238. [PubMed: 12794560]

2. Centers for Disease Control and Prevention. Enhanced Perinatal Surveillance-Participating areas in the United States and dependent areas, 2000–2003. HIV/AIDS Surveillance Supplemental Report. 2009

3. Centers for Disease Control and Prevention. Enhanced perinatal surveillance – 15 areas, 2005–2008. HIV Surveillance Supplemental. 2011

4. European Mode of Delivery Collaboration. Elective caesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. Lancet. 1999; 353:1035–1039. [PubMed: 10199349]

5. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1: a meta-analysis of 15 prospective cohort studies. The International Perinatal HIV Group. N Engl J Med. 1999; 340:977–987. [PubMed: 10099139]

6. Committee on Obstetric Practice. ACOG committee opinion scheduled Cesarean delivery and the prevention of vertical transmission of HIV infection. Number 234, May 2000 (replaces number 219, August 1999). Int J Gynecol Obstet. 2001; 73:279–281.

7. Centers for Disease Control and Prevention. US Public Health Service Task Force recommendations for use of antiretroviral drugs in pregnant HIV-1 infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. MMWR Recomm Rep. 2002; 51:1–38.

8. Meikle SF, Steiner CA, Zhang J, Lawrence WL. A national estimate of the elective primary cesarean delivery rate. Obstet Gynecol. 2005; 105:751–756. [PubMed: 15802401]

9. Newell ML, Thorne C. European HIV in Obstetrics Group. Higher rates of postpartum complications in HIV-infected than in uninfected women irrespective of mode of delivery. AIDS. 2004; 18:933–938. [PubMed: 15060441]

10. Ferrero S, Bentivoglio G. Postoperative complications after caesarean section in HIV-infected women. Arch Gynecol Obstet. 2003; 268:268–273. [PubMed: 14504867]

11. Grubert TA, Reindell D, Kästner R, Lutz-Friedrich R, Belohradsky BH, Dathe O. Complications after caesarean section in HIV-1-infected women not taking antiretroviral treatment. Lancet. 1999; 354:1612–1613. [PubMed: 10560681]

12. Maiques-Montesinos V, Cervera-Sanchez J, Bellver-Pradas J, Abad-Carrascosa A, Serra-Serra V. Postcesarean section morbidity in HIV-positive women. Acta Obstetricia et Gynecologica Scandinavica. 1999; 78:789–792. [PubMed: 10535342]

13. Semprini AE, Castagna C, Ravizza M, Fiore S, Savasi V, Muggiasca ML, et al. The incidence of complications after caesarean section in 156 HIV-positive women. AIDS. 1995; 9:913–917. [PubMed: 7576327]

14. Vimercati A, Greco P, Loverro G, Lopalco PL, Pansini V, Selvaggi L. Maternal complications after caesarean section in HIV infected women. Eur J Obstet Gynecol Reprod Biol. 2000; 90:73–76. [PubMed: 10767514]

15. Rodriguez EJ, Spann C, Jamieson D, Lindsay M. Postoperative morbidity associated with cesarean delivery among human immunodeficiency virus-seropositive women. Am J Obstet Gynecol. 2001; 184:1108–1111. [PubMed: 11349171]

16. Louis J, Landon MB, Gersnoviez RJ, Leveno KJ, Spong CY, Rouse DJ, et al. Perioperative morbidity and mortality among human immunodeficiency virus infected women undergoing cesarean delivery. Obstet Gynecol. 2007; 110(2 Pt 1):385– 390. [PubMed: 17666615]

17. Marcollet A, Goffinet F, Firtion G, Pannier E, Le Bret T, Brival ML, Mandelbrot L. Differences in postpartum morbidity in women who are infected with the human immunodeficiency virus after elective cesarean delivery, emergency cesarean delivery, or vaginal delivery. Am J Obstet Gynecol. 2002; 186:784–789. [PubMed: 11967508]

18. Watts DH, Lambert JS, Stiehm ER, Bethel J, Whitehouse J, Fowler MG, Read J. Complications according to mode of delivery among human immunodeficiency virus-infected women with CD4 lymphocyte counts of < or = 500/microL. Am J Obstet Gynecol. 2000; 183:100–107. [PubMed: 10920316]

19. Read JS, Tuomala R, Kpamegan E, Zorrilla C, Landesman S, Brown G, et al. Mode of delivery and postpartum morbidity among HIV-infected women: the women and infants transmission study. J Acquir Immune Defic Syndr. 2001; 26:236–245. [PubMed: 11242196]

20. Nielsen TF, Hokegard KH. Postoperative cesarean section morbidity: a prospective study. Am J Obstet Gynecol. 1983; 146:911–916. [PubMed: 6881224]

21. Read JS, Newell MK. Efficacy and safety of cesarean delivery for prevention of mother-to-child transmission of HIV-1. Cochrane Database Syst Rev. 2005:CD005479. [PubMed: 16235405]

22. Legardy-Williams JK, Jamieson DJ, Read JS. Prevention of mother-to-child transmission of HIV-1: the role of cesarean delivery. Clin Perinatol. 2010; 37:777ix–785ix. [PubMed: 21078450]

23. Garcia-Tejedor A, Maiques V, Perales A, Lopez-Aldeguer J. Influence of highly active antiretroviral treatment (HAART) on risk factors for vertical HIV transmission. Acta Obstet Gynecol Scand. 2009; 88:882–887. [PubMed: 19557554]

24. Townsend CL, Cortina-Borja M, Peckham CS, de Ruiter A, Lyall H, Tookey PA. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000–2006. AIDS. 2008; 22:973–981. [PubMed: 18453857]

25. Warszawski J, Tubiana R, Le Chenadec J, Blanche S, Teglas JP, Dollfus C, et al. Mother-to-child HIV transmission despite antiretroviral therapy in the ANRS French Perinatal Cohort. AIDS. 2008; 22:289–299. [PubMed: 18097232]

26. Boer K, England K, Godfried MH, Thorne C. European Collaborative Study. Mode of delivery in HIV-infected pregnant women and prevention of mother-to-child transmission: changing practices in Western Europe. HIV Med. 2010; 11:368–378. [PubMed: 20059573]

27. Ioannidis JP, Abrams EJ, Ammann A, Bulterys M, Goedert JJ, Gray L, et al. Perinatal transmission of human immunodeficiency virus type 1 by pregnant women with RNA virus loads <1000 copies/ml. J Infect Dis. 2001; 183:539–545. [PubMed: 11170978]

28. European Collaborative Study. Mother-to-child transmission of HIV infection in the era of highly active antiretroviral therapy. Clin Infect Dis. 2005; 40:458–465. [PubMed: 15668871]

29. Mofenson LM, Lambert JS, Stiehm ER, Bethel J, Meyer WA 3rd, Whitehouse J, et al. Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. N Engl J Med. 1999; 341:385–393. [PubMed: 10432323]

30. Maiques V, Garcia-Tejedor A, Diago V, Molina JM, Borras D, Perales-Puchalt A, Perales A. Perioperative cesarean delivery morbidity among HIV-infected women under highly active antiretroviral treatment: a case-control study. Eur J Obstet Gynecol Reprod Biol. 2010; 153:27–31. [PubMed: 20675036]

31. Landers DV, Duarte G. Mode of delivery and the risk of vertical transmission of HIV-1. N Engl J Med. 1999; 341 205author reply 206–207.

32. Stringer JS, Rouse DJ, Goldenberg RL. Prophylactic cesarean delivery for the prevention of perinatal human immunodeficiency virus transmission: the case for restraint. JAMA. 1999; 281:1946–1949. [PubMed: 10349900]

33. Senise J, Bonafe S, Castelo A. The management of HIV-infected pregnant women. Curr Opin Obstet Gynecol. 2012; 24:395– 401. [PubMed: 23160458]

34. Agency for Healthcare Research and Quality. Overview of the Nationwide Inpatient Sample (NIS) Healthcare Cost and Utilization Project (HCUP). http://www.hcup-us.ahrq.gov/nisoverview.jsp.

35. Gregory KD, Korst LM, Gornbein JA, Platt LD. Using administrative data to identify indications for elective primary cesarean delivery. Health Serv Res. 2002; 37:1387–1401. [PubMed: 12479502]

36. Kourtis AP, Bansil P, McPheeters M, Meikle SF, Posner SF, Jamieson DJ. Hospitalizations of pregnant HIV-infected women in the USA prior to and during the era of HAART, 1994–2003. AIDS. 2006; 20:1823–1831. [PubMed: 16954723]

37. Lapaire O, Irion O, Koch-Holch A, Holzgreve W, Rudin C, Hoesli I. Swiss Mother and Child HIV Cohort Study. Increased peri- and postelective cesarean section morbidity in women infected with human immunodeficiency virus-1: a case-controlled multicenter study. Arch Gynecol Obstet. 2006; 274:165–169. [PubMed: 16715290]

38. Briand N, Jasseron C, Sibiude J, Azria E, Pollet J, Hammou Y, et al. Cesarean section for HIV-infected women in the combination antiretroviral therapies era, 2000–2010. Am J Obstet Gynecol. 2013; 209:335-e1. [PubMed: 23791563]

39. Calvert C, Ronsmans C. HIV and the risk of direct obstetric complications: a systematic review and meta-analysis. PLoS One. 2013; 8:e74848. [PubMed: 24124458]

40. Chama CM, Morrupa JY. The safety of elective caesarean section for the prevention of mother-to-child transmission of HIV-1. J Obstet Gynaecol. 2008; 28:194–197. [PubMed: 18393018]

41. Whitmore SK, Taylor AW, Espinoza L, Shouse RL, Lampe MA, Nesheim S. Correlates of mother-to-child transmission of HIV in the United States and Puerto Rico. Pediatrics. 2012; 129:e74–e81. [PubMed: 22144694]

42. Williams PL, Seage GR 3rd, Van Dyke RB, Siberry GK, Griner R, Tassiopoulos K. A trigger-based design for evaluating the safety of in utero antiretroviral exposure in uninfected children of human immunodeficiency virus-infected mothers. Am J Epidemiol. 2012; 175:950–961. [PubMed: 22491086]

43. Merrill, C.; Steiner, C. Rockville (MD): Agency for Health Care Policy and Research (US); 2006 Feb. Hospitalizations related to childbirth, 2003. Statistical Brief #11. 2006 Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. Available at: http://www.ncbi.nlm.nih.gov/books/NBK63491/ [Accessed 1 May 2014]
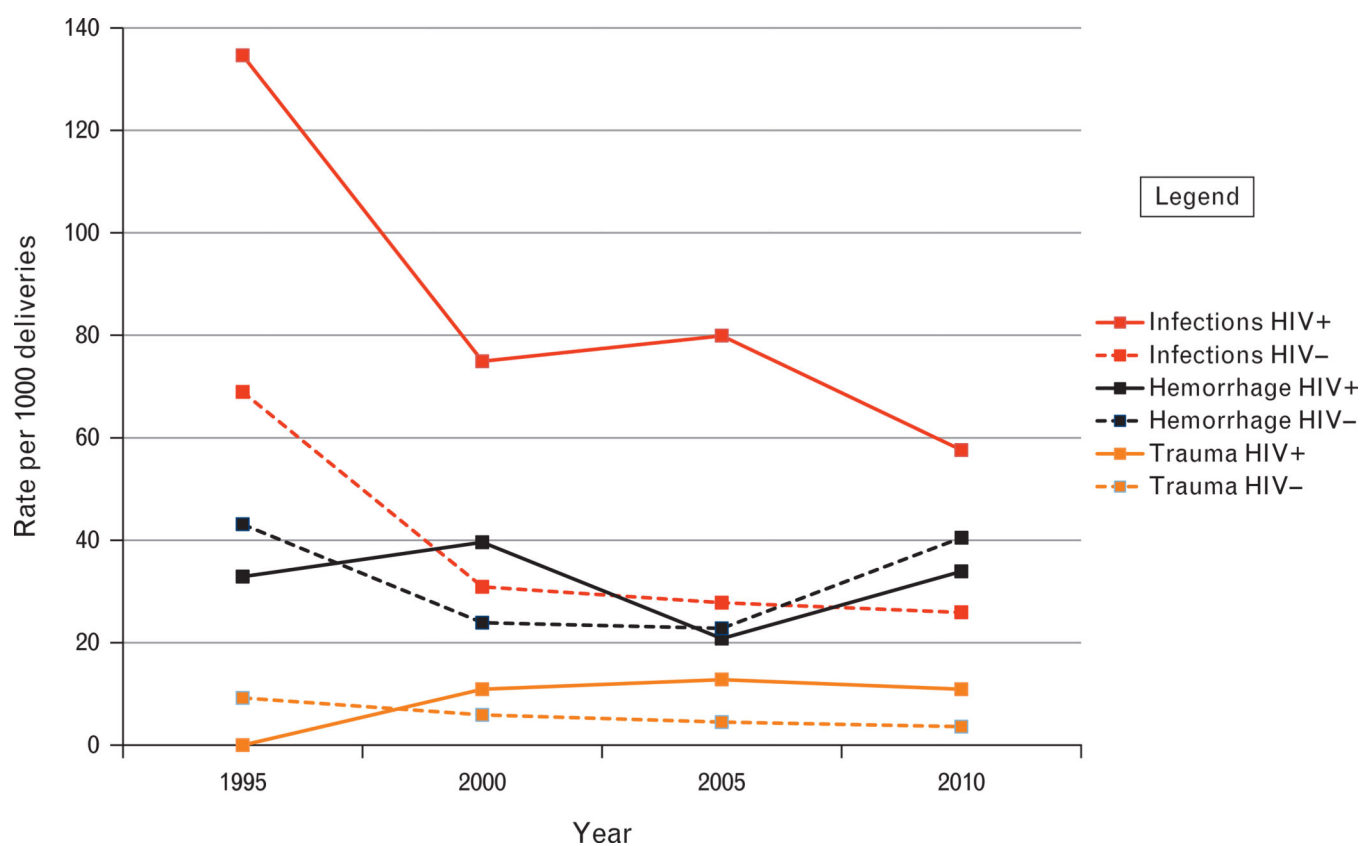
Fig. 1.
Trends in the rate of infection, hemorrhage and surgical trauma associated with cesarean deliveries in the United States, by HIV status, 1995, 2000, 2005, and 2010 Nationwide Inpatient Sample.

Table 1

Distribution of patient, hospital, and key characteristics of cesarean delivery hospitalizations, by HIV status–United States, 1995 and 2010.

| | 1995 | | | | | | 2010 | | | | | |
| | Cesarean deliveries | | | Elective cesarean deliveries | | | Cesarean deliveries | | | Elective cesarean deliveries | | |
	HIV+	HIV− n (% of all deliveries)	P	HIV+	HIV− n (% of all deliveries)	P	HIV+	HIV− n (% of all deliveries)	P	HIV+	HIV− n (% of all deliveries)	P
Total n	934	799 707		416	368 790		2798	1 270 952		2544	929 111	
Patient age												
15–19	74 (7.9%)	70 245 (8.8%)	0.0352	16 (3.9%)	21 558 (5.8%)	0.0173	169 (6.1%)	82 556 (6.5%)	0.8182	133 (5.2%)	44 071 (4.7%)	0.8346
20–34	753 (80.7%)	593 439 (74.2%)		355 (85.4%)	273 441 (74.1%)		2064 (73.8%)	947 268 (74.5)		1883 (74.0%)	691 823 (74.5%)	
35–49	106 (11.4%)	136 024 (17.0%)		45 (10.7%)	73 791 (20.0%)		564 (20.2%)	241 127 (19.0%)		527 (20.7%)	193 218 (20.8%)	
Diabetes												
Yes	40 (4.2%)	49 590 (6.2%)	0.1185	18 (4.4%)	24 617 (6.7%)	0.3631	222 (7.9%)	127 217 (10.0%)	0.0866	201 (7.9%)	96 663 (10.4%)	0.0413
Anemia												
Yes	378 (40.5%)	119 842 (15.0%)	0.0427	144 (34.5%)	53 161 (14.4%)	0.0642	820 (29.3%)	205 103 (16.1%)	<0.0001	758 (29.8%)	145 420 (15.7%)	<0.0001
Alcohol/substance abuse												
Yes	168 (18.0%)	17 922 (2.2%)	0.0002	74 (17.9%)	9953 (2.70%)	0.008	207 (7.4%)	21 330 (1.7%)	0.0045	207 (8.1%)	17 162 (1.8%)	0.0045
Primary expected payer												
Public (Medicaid or Medicare)	687 (73.6%)	278 676 (35.1%)	<0.0001	299 (72.0%)	124 682 (34.1%)	0.0004	2013 (72.1%)	554 377 (43.7%)	0.0001	1827 (72.0%)	407 360 (43.9%)	0.0001
Private, include HMO	106 (11.4%)	462 087 (58.2%)		53 (12.8%)	217 365 (59.4%)		575 (20.6%)	642 859 (50.7%)		523 (20.6%)	467 534 (50.4%)	
Other, including self-pay	140 (15.0%)	53 227 (6.7%)		64 (15.3%)	23 902 (6.5%)		205 (7.3%)	71 865 (5.7%)		189 (7.4%)	52 913 (5.7%)	
Hospital teaching status/location												
Rural	37 (4.0%)	105 774 (13.3%)	0.0256	4 (1.1%)	49 539 (13.5%)	0.0007	105 (3.8%)	139 709 (11.2%)	0.0003	95 (3.7%)	100 454 (11.0%)	0.0003
Urban, nonteaching	321 (34.7%)	411 037 (51.6%)		183 (44.7%)	192 136 (52.4%)		322 (11.6%)	532 113 (42.6%)		288 (11.4%)	388 719 (42.6%)	
Urban-teaching	568 (61.3%)	279 467 (35.1%)		221 (54.2%)	124 984 (34.1%)		2349 (84.6%)	576 542 (46.2%)		2146 (84.9%)	423 158 (46.4%)	
Hospital region												
Northeast	126 (13.5%)	154 029 (19.3%)	0.0017	75 (18.1%)	71 746 (19.5%)	0.0067	602 (21.5%)	207 008 (16.3%)	0.0022	529 (20.8%)	153 022 (16.5%)	0.002
Midwest	50 (5.3%)	176 102 (22.0%)		33 (7.8%)	85 409 (23.20%)		256 (9.2%)	258 595 (20.4%)		230 (9.1%)	188 030 (20.20%)	

| | 1995 | | | | | | 2010 | | | | | |
| | Cesarean deliveries | | | Elective cesarean deliveries | | | Cesarean deliveries | | | Elective cesarean deliveries | | |
	HIV+	n (% of all deliveries) HIV−	P	HIV+	n (% of all deliveries) HIV−	P	HIV+	n (% of all deliveries) HIV−	P	HIV+	n (% of all deliveries) HIV−	P
South	736 (78.9%)	269 448 (33.7%)		290 (69.9%)	122 964 (33.30%)		1735 (62.0%)	519 480 (40.9%)		1605 (63.1%)	384 053 (41.3%)	
West	22 (2.4%)	200 128 (25.0%)	0.0004	17 (4.20%)	88 671 (24.00%)	0.0078	204 (7.3%)	285 870 (22.5%)	<0.0001	179 (7.00%)	204 006 (22.0%)	<0.0001
Length of stay[a] (days)	5.2	3.6	0.0004	5.9	3.6	0.0078	4.3	3.6	<0.0001	4.3	3.5	<0.0001
Charges[a] (2010 $)	15 507	10 403	0.0003	17 519	9995	0.0072	22 168	19 253	0.0004	22 101	18 642	<0.0001

[a] Mean and Satterthwaite P values reported for continuous variables

Table 2

Rates[a] and adjusted odds ratios of cesarean delivery-associated complications, extended hospital stays, and in-hospital deaths, by HIV status and cesarean delivery type (all caesarean deliveries and elective cesarean deliveries) 1995–1996 and 2010–2011.

Complication	All cesarean deliveries rate (n^b)				Elective cesarean deliveries			
	HIV+	HIV–	aOR[c]	95% CI	HIV+	HIV–	aOR[c]	95% CI
1995/1996								
Any complication[d]	210.6 (430)	118.9 (189 197)	1.00	(.68, 1.49)	245.1 (240)	109.3 (80 324)	1.59	(.99, 2.54)
Infection	143.0 (292)	69.1 (109 928)	1.36	(1.03, 1.80)	181.2 (178)	62.3 (45 770)	2.08	(1.45, 2.98)
Hemorrhage	68.1 (139)	47.1 (74 975)	0.66	(.40, 1.10)	58.6 (57)	43.8 (32 215)	0.64	(.33, 1.26)
Surgical trauma	_[e]	9.7 (15 395)	0.56	(.16, 1.91)	–	9.5 (6974)	0.34	(0.047, 2.52)
Hospital stay >7 days	112.1 (229)	33.1 (52 711)	2.04	(1.38, 3.02)	127.0 (125)	38.3 (28 163)	2.35	(1.35, 4.07)
Deaths	–	0.28 (443)	13.17	(3.57, 48.56)	–	0.37 (270)	20.40	(5.16, 80.57)
Charges[f]	15 971 (13 631–18 312)	10 484 (10 450–10 519)		<0.001	17 597 (13 017–22 177)	10 062 (10 004–10 119)		0.0014
2010/2011								
Any complication[d]	116.6 (589)	67.9 (172 334)	1.03	(.75, 1.42)	113.9 (520)	62.4 (115 611)	1.05	(.76, 1.45)
Infection	59.2 (299)	25.3 (64 260)	1.66	(1.18, 2.35)	56.9 (260)	22.3 (41 388)	1.70	(1.19, 2.42)
Hemorrhage	50.1 (253)	42.3 (107 228)	0.56	(.40, 0.80)	48.0 (219)	39.4 (72 963)	0.56	(.38, 0.82)
Surgical trauma	12.8 (65)	3.7 (9403)	2.45	(1.41, 4.26)	14.1 (65)	3.6 (6740)	2.71	(1.56, 4.71)
Hospital stay >7 days	71.8 (363)	24.4 (62 031)	2.09	(1.58, 2.74)	74.9 (342)	27.6 (51 075)	1.96	(1.47, 2.60)
Deaths	–	0.16 (401)	9.06	(2.6, 31.58)	–	0.20 (364)	8.74	(2.52, 30.24)
Charges[f]	24 063(22 483–25 643)	19 359 (19 311–19 407)		<0.001	23 966 (22 267–25 665)	18 773 (18 714–18 832)		<0.001

aOR, adjusted odds ratio; CI, confidence interval.

[a]Rates are per 1000 deliveries.

[b]Number of incidents used for rate calculation.

[c]Adjusted for patient age, primary expected payer, hospital teaching status/location, hospital region, alcohol/substance abuse, diabetes, and anemia.

[d]Any complication includes infection, hemorrhage, thrombosis or surgical trauma, as defined in Methods.

[e]Cells with dashes are not reported due to low cell counts.

[f]Means with 95% CI and Satterthwaite *P* values reported.

Table 3

Multivariable logistic and linear regression analysis for cesarean delivery-related complications, extended hospital stays, and deaths, and mean charges among HIV-infected and HIV-uninfected women, 1995/1996, 2000/2001, 2005/2006 and 2010/2011.

	aOR (95% CI)[a]			
	1995/1996 (REF)	**2000/2001**	**2005/2006**	**2010/2011**
All cesarean deliveries				
HIV-infected				
Any complication	1.0	0.84 (0.54–1.30)	0.57 (0.37–0.88)	0.53 (0.33–0.88)
Infection	1.0	0.90 (0.60–1.33)	0.59 (0.40–0.86)	0.42 (0.27–0.66)
Hemorrhage	1.0	0.67 (0.27–1.64)	0.47 (0.18–1.22)	0.76 (0.31–1.86)
Surgical trauma	1.0	1.85 (0.43–8.00)	1.87 (0.44–8.01)	2.18 (.53–9.06)
Hospital stay >7 days	1.0	0.41 (0.25–0.69)	0.42 (0.26–0.66)	0.56 (0.35–0.91)
Deaths	1.0	–	0.08 (0.01–1.11)	0.37 (0.05–2.60)
Adjusted mean charges (95% CI)[b]	$15 793 (13 156–18 431)	$14 154 (12 872–15 435)	$16 882 (15 538–18 226)	$24 104 (21 281–26 926)
HIV-uninfected				
Any complication	1.0	0.74 (0.68–0.81)	0.44 (0.40–0.48)	0.44 (0.39–0.50)
Infection	1.0	0.81 (0.74–0.88)	0.44 (0.41–0.48)	0.32 (0.29–0.35)
Hemorrhage	1.0	0.65 (0.54–.77)	0.51 (0.42–.62)	0.78 (0.62–0.99)
Surgical trauma	1.0	0.56 (0.50–0.65)	0.44 (0.39–0.50)	0.36 (0.31–0.40)
Hospital stay >7 days	1.0	0.83 (0.75–0.91)	0.70 (0.64–0.77)	0.61 (0.55–0.67)
Deaths	1.0	0.81 (0.58–1.15)	0.52 (0.37–.72)	0.47 (0.34–0.66)
Adjusted mean charges (95% CI)[b]	$10 425 (10 172–10 678)	$12 460 (11 975–12 944)	$15 164 (14 654–15 675)	$19 189 (18 411–19 967)
Elective cesarean deliveries				
HIV-infected				
Any complication	1.0	0.57 (0.36–0.91)	0.39 (0.24–0.63)	0.39 (0.23–0.65)
Infection	1.0	0.59 (0.39–0.91)	0.41 (0.26–0.63)	0.30 (0.18–0.49)
Hemorrhage	1.0	0.55 (0.20–1.55)	0.39 (0.13–1.21)	0.65 (0.23–1.84)
Surgical trauma	1.0	4.14 (0.48–35.9)	3.20 (0.35–29.1)	4.73 (0.56–39.9)
Hospital stay >7 days	1.0	0.32 (0.17–0.61)	0.35 (0.20–0.64)	0.49 (0.27–0.89)
Deaths	1.0	–	0.05 (0.004–66)	0.23 (0.04–1.50)
Adjusted mean charges (95% CI)[b]	$17 391 (12848–21 934)	$13 840 (12478–15 203)	$16 686 (15 243–18 128)	$23 932 (21 122–26 741)
HIV-uninfected				
Any complication	1.0	0.78 (0.71–0.84)	0.42 (0.39–0.46)	0.44 (0.39–0.49)
Infection	1.0	0.85 (0.78–0.93)	0.42 (0.38–0.45)	0.30 (0.28–0.33)
Hemorrhage	1.0	0.64 (0.54–0.76)	0.50 (0.41–0.30)	0.77 (0.62–0.97)
Surgical trauma	1.0	0.56 (0.49–0.64)	0.44 (0.38–0.51)	0.35 (0.31–0.40)
Hospital stay >7 days	1.0	0.84 (0.75–0.93)	0.68 (0.62–0.78)	0.59 (0.53–0.65)
Deaths	1.0	0.79 (0.53–1.18)	0.50 (0.34–0.73)	0.43 (0.29–0.64)

	aOR (95% CI)[a]			
	1995/1996 (REF)	**2000/2001**	**2005/2006**	**2010/2011**
Adjusted mean charges (95% CI)[b]	$10 072 (9803–10 342)	$12 091 (11643–12 538)	$14 778 (14260–15 295)	$18 571 (17 807–19 336)

Results also shown for elective cesarean deliveries. aOR, adjusted odds ratio; CI, confidence interval; REF, referent group.

[a]Adjusted for age group, primary expected payer, hospital teaching status/location, hospital region, alcohol/substance abuse, anemia and diabetes.

[b]Multiple linear regression adjusted for age group, primary expected payer, hospital teaching status/location, hospital region, alcohol/substance abuse, anemia and diabetes.